LETTERS TO THE EDITOR

Regarding "Optimal statin type and dosage for vascular patients"

Paraskevas et al[1] are claiming that rosuvastatin or atorvastatin is the optimal statin at a dose of ≥20 mg/d for vascular patients. Epidemiologic studies showed that a low level of high-density lipoprotein cholesterol (HDL-C; <1.0 mmol/L or 40 mg/dL), independent of low-density lipoprotein cholesterol (LDL-C), is a marker of cardiovascular risk.[2] Despite the known efficacy of the various statins to increase HDL-C, the interindividual response is rather high and unpredictable. Therefore, the optimal HDL-C–elevating statin in a particular patient cannot be predicted.

The authors state that statin-induced adverse events may be dose-related, which is substantiated by large trials. However, it is well known that these studies underestimate side effects, partly because the exclusion criteria avoid to a large extent possible drug interactions. Especially side effects, such as mild myopathies, have not been specifically questioned and documented. No data from comparative trial investigating muscular side effects are available yet.

In >1000 patients admitted to our lipid unit because of side effects, the prevalence of myopathy exactly reflected the frequency that the respective statins were prescribed at that time (Table).[3] A creatine kinase increase (>5-fold) on statin monotherapy was extremely rare (16 of 1111 patients). Therefore, there is no evidence that atorvastatin is associated with the highest and fluvastatin with the lowest risk of adverse events.

The assumption that milder side effects of certain statins are counterbalanced by their lower efficacy is not evidence-based. With the option of a weekly dosing of a long half-life statin for statin-intolerant patients, the authors contradict their own assertion that only the most potent statins at ≥20 mg/d are appropriate for vascular patients. Furthermore, statin-intolerant patients who do not tolerate any lipid-lowering agent, even on alternate-day dosing, should therefore undergo LDL apheresis, according to the respective national guidelines.

In our unit in ~50% of patients with clinically symptomatic and proven atherosclerosis, other statins than rosuvastatin and atorvastatin are effective to achieve target values according to the guidelines. A ≥40% decrease in LDL-C has been described as being necessary to induce regression of atherosclerosis.[4] A long-term lesion stabilization achieved by LDL-lowering to target values may be sufficient. What is the clinical proof concerning the cardiovascular event rate for the ≥40% LDL-lowering? Interindividual response to various statins varies considerably, not allowing preferential recommendations.

Moreover, statins have pleiotropic effects, independent of changes in serum cholesterol, not considered by Paraskevas et al,[1] including improving endothelial function, exerting anti-inflammatory actions, and stabilizing atherosclerotic plaques.[5] Furthermore, no statement on combination treatment, which would also allow achieving the goal with other statins, is given.

In some patients, extremely elevated lipoprotein(a) (>100 mg/dL), cigarette smoking, or other risk factors despite normal lipids, are the key pathogenetic mechanisms for the development of vascular disease. These patients do not fit into the therapeutic recommendations at all.

We agree with a key statement that adherence to statin therapy is the central problem to be addressed in this group of patients. However, we do not believe that this simple statin type and dose recommendation for vascular disease patients is justified at present.

Table. The prevalence of myopathy exactly reflected the frequency that the respective statin was prescribed[a]

Statin	*Patients no. (%)*	*Myopathies (%)*
Patient total	1111	
Simvastatin	400 (36.01)	34.80
Atorvastatin	396 (35.64)	37.20
Fluvastatin	156 (14.04)	14.00
Pravastatin	111 (9.99)	11.80
Lovastatin	41 (3.69)	0.70
Rosuvastatin	7 (0.63)	1.50

[a]Unpublished data.

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Reply

Berent and Sinzinger[1] raise many, mostly questionable points. First, regarding their comment that a low level of high-density lipoprotein cholesterol (HDL-C) is a marker of cardiovascular risk independent of low-density lipoprotein cholesterol (LDL-C) levels, a recent systematic review and meta-regression analysis of 108 studies, including 299,310 participants, showed that by increasing HDL-C levels, there is no reduction in the risk of coronary heart disease events, coronary heart disease deaths, or total deaths.[2] This meta-analysis concluded that a reduction in LDL-C levels should be the primary goal for lipid-modifying interventions.[2]

Second, the response of patients varies with ***all*** drugs; we suggested statin types and dosages that are more likely to achieve guideline targets.[3] There will also always be variations in statin use. Surely, Berent and Sinzinger do not advocate a random choice of statin types and dosages.

Third, they question the statement that statin-induced "myopathy" is dose-related and mention that "especially side effects, such as mild myopathies, have not been specifically questioned and documented."[1] The authors seem not to be aware of a study published last year, the Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (SEARCH). This study, comprising 12,064 participants, showed that the incidence of myopathy was 30-fold greater in patients taking 80 mg compared with 20 mg of simvastatin.[4]